Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dolocopin 40mg/g Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 gram of cream contains 40 mg of lidocaine.

Excipients with known effect:
1 gram of cream contains 75mg of propylene glycol
1 gram of cream contains 15mg of benzyl alcohol
1 gram of cream contains 73.2mg of hydrogenated soy lecithin
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cream
A white to off-white yellowish cream

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Local anaesthetic for topical use to produce surface anaesthesia of the skin prior to:
- venous cannulation or venipuncture in adults and in the paediatric population ≥ one month
- administration of painful topical treatments on larger surface areas of intact skin where use of a topical anaesthetic is appropriate in adults only.

4.2 Posology and method of administration

For cutaneous use only.

Venous cannulation or venipuncture:

Posology:
Adults, including elderly, and children over one month of age:

Paediatric Population:
Use of Dolocopinis not recommended for this indication in infants under one month of age.

Method of administration:
Apply 1g to 2.5g of cream onto the skin to cover a 2.5cm x 2.5cm (6.25cm^2) area where venous cannulation or venipuncture will occur. No more than 1g of cream should be applied to infants below the age of 1 year. 1g of cream equates to approximately 5cm of cream squeezed from the 5g tube, or 3.5cm from the 30g tube.

The cream should remain undisturbed and the area can be covered with an occlusive dressing to prevent disturbance or interference by the patient or other external factors. Adequate anaesthesia should be obtained after 30 minutes, but the Dolocopinmay be applied for up to 5 hours under a dressing. Prior to starting the procedure, the Dolocopinshould be removed using a clean gauze swab and the site for venous cannulation or venipuncture prepared in the usual manner. The procedure should be initiated shortly after the cream has been removed. Maximum application time for 1 month upto 3 month infant should not exceed 60 minutes. Maximum application time for 3 month upto 12 month infant should not exceed 4 hours. Maximum application for 12 month infant – adult should not exceed 5 hours.

Painful topical treatments on larger surface areas of intact skin:

Posology:

Adults, including the elderly

Paediatric Population:
Use of Dolocopinis not recommended for this indication in patients below 18 years of age.

Method of administration:
Apply the cream at a dosage of approximately 1.5g to 2g Dolocopin/10cm^2 skin to be treated, or multiples thereof, up to a maximum area of 300cm2. Apply until response is achieved, which is generally for between 30 to 60 minutes in clinical studies.

Typical estimated larger quantities would be 30g-40g/200cm2 (approximately 10cm x 20cm, or covering a face), 45g-60g/300cm^2 (approximately 10cm x 30cm or covering an arm).

Indirect evidence has shown that successive applications of lidocaine-based topical treatments can lead to systemic accumulation of lidocaine.
Dolocopinmust therefore not be reapplied for 12 hours following its removal, giving a maximum of 2 doses in any 24 hour period.

The Dolocopin should be applied evenly at the specified dosage with a uniform thickness across the area where the topical treatment will occur. Measures may be taken to ensure the cream remains undisturbed until adequate analgesia has been achieved.

Prior to starting the procedure, the Dolocopin should be removed using a clean gauze swab and the site for topical treatment prepared in the usual manner. The procedure should be initiated shortly after the cream has been removed.

4.3 Contraindications

Hypersensitivity to the active substance, or any of the amide-type local anaesthetics, or to any of the excipients listed in Section 6.1.

Hypersensitivity to soya or peanuts.

4.4 Special warnings and precautions for use

For external use only.

Avoid contact with eyes.

Do not apply to irritated skin or if excessive irritation develops. If condition worsens, or if symptoms persist unaltered for more than seven days or clear up and occur again within only a few days, discontinue use of this product and consult a doctor.

Do not use in large quantities over raw or blistered areas.

Dolocopin contains 75mg propylene glycol in each 1g. Propylene glycol may cause skin irritation.

Dolocopin has not been applied to wounds, mucous membranes or in areas of atopic dermatitis as there are no clinical data in relation to these.

Dolocopin contains 15mg benzyl alcohol in each 1g. Benzyl alcohol may cause allergic reactions or mild local irritation.

Dolocopin contains hydrogenated soy lecithin. If you are allergic to peanut or soya, do not use this medicinal product.

Application of lidocaine to larger areas or for longer times than those recommended could result in sufficient absorption of lidocaine resulting in serious adverse effects.

Studies in laboratory animals (guinea pigs) have shown that lidocaine has an ototoxic effect when instilled into the middle ear. In these same studies, animals exposed to lidocaine in the external auditory canal only showed no abnormality. Lidocaine should not be used in any clinical situation in which its penetration or migration beyond the tympanic membrane into the middle ear is possible.

Dermal application of lidocaine may cause transient local blanching followed by transient erythema.

PRECAUTIONS

General: Repeated doses of lidocaine may increase blood levels of lidocaine. Lidocaine should be used with caution in patients who may be more sensitive to the systemic effects of lidocaine including acutely ill, debilitated, or elderly patients.

Lidocaine coming in contact with the eye should be avoided because animal studies have demonstrated severe eye irritation. Also the loss of protective reflexes can permit corneal irritation and potential abrasion. Absorption of lidocaine in conjunctival tissues has not been determined. If eye contact occurs, immediately wash out the eye with water or saline and protect the eye until sensation returns.

Patients allergic to para-aminobenzoic acid derivatives (procaine, tetracaine, benzocaine, etc.) have not shown cross sensitivity to lidocaine; however, lidocaine should be used with caution in patients with a history of drug sensitivities, especially if the etiologic agent is uncertain. Patients with severe hepatic disease, because of their inability to metabolize local anaesthetics normally, are at greater risk of developing toxic plasma concentrations of lidocaine.

When lidocaine is used, the patient should be aware that the production of dermal analgesia may be accompanied by the block of all sensations in the treated skin. For this reason, the patient should avoid inadvertent trauma to the treated area by scratching, rubbing, or exposure to extreme hot or cold temperatures until complete sensation has returned.

Lidocaine has bactericidal and antiviral properties in concentrations above 0.5%. For this reason, the results of intra-cutaneous injections of live vaccines (such as BCG vaccination) should be monitored.

Patients treated with Class III anti-arrhythmic drugs (e.g. amiodarone) should be carefully monitored and ECG monitoring considered as cardiac effects may be additive.

Paediatric population
Anaesthetic efficacy during the heel lancing of neonates has not been studied.

4.5 Interaction with other medicinal products and other forms of interaction

Lidocaine should be used with caution in patients receiving Class I and Class III anti-arrhythmic drugs (such as tocainide and mexiletine) since the toxic effects are additive and generally synergistic.

Drugs that reduce the clearance of lidocaine (eg cimetidine or betablockers, such as propranolol) may cause potentially toxic plasma concentrations when lidocaine is given in repeated high doses over a long period of time. Such interactions should therefore be of no clinical importance following short term treatment with lidocaine (eg Dolocopin) at recommended doses.

The risk of additional systemic toxicity should be considered when large doses of Dolocopin are applied to patients already using other local anaesthetics.

Paediatric Population
Specific interaction studies in children have not been performed. Interactions are likely to be similar to the adult population.

4.6 Fertility, pregnancy and lactation

Pregnancy
Although topical application of lidocaine is associated with only a low level of systemic absorption, the use of Dolocopin in pregnant women should be undertaken with care because there are no, or limited, adequate and well-controlled studies in pregnant patients. Animal studies are insufficient with respect to reproductive toxicity, however they do not indicate any direct or indirect negative effects on pregnancy, embryo-fetal development, parturition or postnatal development. Reproduction toxicity has been shown with subcutaneous/intramuscular administration of high doses of lidocaine much exceeding the exposure from topical application (see section 5.3).

Lidocaine can cross the placental barrier and may be absorbed by the fetal tissues. It is reasonable to assume that lidocaine has been used in a large number of pregnant women and women of childbearing age. No specific disturbances to the reproductive process have so far been reported, e.g. an increased incidence of malformations or other directly or indirectly harmful effects on the fetus.

Breast-feeding

Lidocaine is excreted in breast milk, but in such small quantities that there is generally no risk of the child being affected at therapeutic dose levels. Dolocopin can be used during breast-feeding if clinically needed.

Fertility
There are no data on the effects of lidocaine on fertility. Animal studies have shown no impairment of the fertility of male or female rats (see section 5.3)

4.7 Effects on ability to drive and use machines

No or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Common side effects can include irritation, redness, itching, or rash.

In rare cases local anaesthetics have been associated with allergic reactions including anaphylactic shock.

Corneal irritation after accidental eye exposure.

System Organ Class	Very Common (≥1/10)	Common ≥1/100, <1/10	Uncommon ≥1/1,000,< 1/100	Rare ≥1/10,000,< 1/1000	Very Rare <1/10,000	Not known (cannot be estimated from available data)
Eye Disorders						Corneal irritation (after accidental eye exposure)
Immune System Disorders				Allergic Reactions Anaphylactic Shock		
Skin and Subcutaneous Tissue Disorders		Irritation Redness Itching Rash				

Paediatric Population
Frequency, type and severity of adverse reactions are similar in the paediatric and adult age groups.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Overdose with Dolocopin is unlikely but signs of systemic toxicity would be consistent with those of lidocaine.

An indication of systemic toxicity may include blurred vision, dizziness or drowsiness, difficulty breathing, trembling, chest pain, or irregular heartbeat.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anaesthetics for topical use, lidocaine, ATC Code: N01BB02

Mechanism of Action and Pharmacodynamic Effects
Dolocopin applied to intact skin provides dermal analgesia by a release of lidocaine from the cream into the epidermal and dermal layers of the skin, and by the accumulation of lidocaine in the vicinity of pain receptors and nerve endings. Lidocaine is an amide-type local anaesthetic agent which stabilises neuronal membranes by inhibiting the ionic fluxes required for the initiation and conduction of impulses, thereby effecting local anaesthetic action. The main action is a blockade of voltage-dependent sodium channels. The onset, depth and duration of dermal analgesia provided by lidocaine depend primarily on the duration of application. Dolocopin may cause transient peripheral vasoconstriction followed by transient vasodilation at the application site.

Clinical Efficacy and Safety
Dolocopin has been shown to provide reliable analgesia when applied for between 30 to 60 minutes in clinical studies. The cream may remain on the skin after this time, if adequate analgesia is not achieved. Caution should be taken particularly when applying Dolocopin onto large areas for longer than for 2 hours.

Local adverse toxicity of Dolocopin has been shown to be low when applied across the proposed dosage range to intact skin. The incidence of systemic adverse reactions can be expected to be directly proportional to the area and time of exposure.

Paediatric Population
In trials focused on children and venipunction, use of Dolocopin was associated with a higher intravenous cannulation success rate, less pain, shorter total procedure time and minor dermal changes among children undergoing cannulation. The incidence of adverse reactions was low.
Dolocopin satisfactorily anaesthetised the skin prior to venipuncture following 30 minutes application time without occlusion in children.

Maximum application time for venous cannulation for 1 month upto 3 month infant should not exceed 60 minutes, for 3 month upto 12 month infant should not exceed 4 hours, and for 12 month infant – adult should not exceed 5 hours.

5.2 Pharmacokinetic properties

Absorption, Distribution, Biotransformation and Elimination
Specific pharmacokinetic studies with Dolocopin in animals have not been performed. However, there is considerable data available on the pharmacokinetic properties of lidocaine deriving from its long-lasting and worldwide use as a local anaesthetic. The amount of lidocaine systemically absorbed is directly related to both the duration of application and to the area over which it is applied. It is not known if it is metabolized into the skin. Lidocaine is metabolized rapidly by the liver to a number of metabolites including monoethylglycinexylidide (MEGX) and glycinexylidide (GX), both of which have pharmacologic activity similar to, but less potent to that of lidocaine. The metabolite, 2,6-xylidine, has unknown pharmacologic activity but is carcinogenic in rats.

Following intravenous administration, MEGX and GX concentrations in serum range from 11 to 36% and from 5 to 11% of concentrations, respectively. The half-life of lidocaine elimination from the plasma following IV administration is approximately 65 to 150 minutes (mean 110, ±24 SD, n=13). This half-life may be increased in cardiac or hepatic dysfunction. More than 98% of an absorbed dose of can be recovered in the urine as metabolites or parent drug. The systemic clearance is 10 to 20 mL/min/kg (mean 13, ±3 SD, n=13).

When applied topically to intact skin, the absorption of lidocaine is very low. Increased absorption is therefore to be expected when applied to mucosa or previously damaged skin.Pharmacokinetic data confirms systemic lidocaine levels to be less than the systemic therapeutic level of 1ug/ml when Dolocopin is applied at the proposed dosage over a range of skin areas.

Paediatric Population
The maximum plasma level of active ingredient was very low (0.3 µg/ml or less) in a study investigating the application of Dolocopin for cannulation in children of different ages. It was well below the toxically effective plasma level of ingredients.

5.3 Preclinical safety data

As yet a detailed toxicological program has not been performed with lidocaine nor with Dolocopin however relevant pre-clinical data is available from a considerable number of individual animal studies.

High amounts of lidocaine entering the circulation can induce symptoms and signs of toxicity, largely emanating from effects on the central nervous system and the cardiovascular system. Since lidocaine readily crosses the placenta, there is also a risk of fetal toxicity. The possibility of adverse fetal effects is further enhanced by fetal acidosis resulting in free drug accumulation in the fetus.

Lidocaine can cause methemoglobinaemia, but the incidence rate is considerably lower than that arising from prilocaine administration and the risk is therefore considered to be extremely low, especially after topical application.

The mutagenic potential of lidocaine has been tested in the Ames Salmonella/mammalian microsome test and by analysis of structural chromosome aberrations in human lymphocytes in vitro, and by mouse micronucleus test in vivo. There was no indication in these tests of any mutagenic effects. A metabolite of lidocaine, 2,6-dimethylaniline showed evidence of genotoxic activity. This metabolite has been shown to have carcinogenicity potential in preclinical toxicological studies evaluating chronic exposure. When applied topically on intact skin the absorption of lidocaine is very low and a significant formation of 2,6-xylidine systemically is not to be expected.

Animal studies on the potential reproductive and developmental toxicity of lidocaine did not provide any evidence for a significant teratogenic potential of lidocaine, but some behavioural effects at high concentration of the local anaesthetic have been demonstrated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl Alcohol
Carbomers
Cholesterol
Hydrogenated Soy Lecithin
Polysorbate 80
Propylene Glycol
Trolamine (for pH adjustment)
all-*rac*-α-Tocopheryl Acetate
Purified Water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Unopened: Three years
Opened: 6 months

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.
For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

The pack sizes are 5g and 30g. Both packs sizes comprise either:
- an aluminium tube with an epoxyphenolic internal lacquer fitted with a polypropylene screw cap or
- an aluminium tube with a polyamide-imide internal lacquer fitted with a high density polyethylene screw cap.

The following packaging options are approved but not all of these packaging options may be marketed:
1) A carton containing one 5g tube.
2) A carton containing five 5g tubes.

3) A carton containing one 5g tube with two Tegaderm® occlusive dressings.
4) A carton containing five 5g tubes with ten Tegaderm® occlusive dressings.
5) A carton containing one 30g tube.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

7 MARKETING AUTHORISATION HOLDER

Ferndale Laboratories Limited
Lee View House
South Terrace
Cork
T12 T0CT
Ireland

8 MARKETING AUTHORISATION NUMBER

PA22869/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27th November 2015
Date of last renewal: 5th October 2020

10 DATE OF REVISION OF THE TEXT

March 2024